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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BURNS DOANE SWECKER & MATHIS L L P			JIANG, SHAOJIA A	
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1617

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/089,449

Applicant(s)

SZELENYI ET AL.

Examiner

Shaojia A Jiang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

This application is a 371, a national stage entry of PCT/EP00/09392 International Filing Date: 09/26/2000 which claims foreign priority to German 199 47 235.1 under 35 U.S.C. 119(a)-(d). The copy of certified copy of the priority has not been filed with the instant Application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 7-8 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the particular $\beta 2$ adrenoceptor agonist, such as salbutamol, reproterol, salmeterol, and formoterol disclosed in the specification herein, does not reasonably provide enablement for any $\beta 2$ adrenoceptor agonists employed in the pharmaceutical composition and the particular method of treatment for asthma or allergy recited in the claims herein.

These recitation, "one $\beta 2$ adrenoceptor agonist", is seen to be merely functional language.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required

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undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a pharmaceutical composition and the particular method of treatment for asthma or allergy.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since these claims read on any compounds having function as β_2 adrenoceptor agonist.

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a

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fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

In the instant case, "one β 2 adrenoceptor agonist", recited in the instant claims is purely functional distinction. Hence, the functional recitation reads on any compounds that might have the recited functions. However, the specification merely provides four particular compound for this functional compounds for the composition and particular method herein.

Thus, Applicants functional language at the points of novelty fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).

The predictability or unpredictability: the instant claimed invention is highly *unpredictable* as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the

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genus, by structure, formula, or chemical name, of the claimed subject matter, as discussed above in *University of California v. Eli Lilly and Co.* Hence, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the pharmaceutical compositions herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects, side effects, and especially serious toxicity that may be generated by drug-drug interactions when and/or after administering to a host (e.g., a human) the **combination** of any compounds represented by “one β_2 adrenoceptor agonist”, and loteprednol, which may encompass more than a thousand compounds. See text book “Goodman & Gilman’s The Pharmacological Basis of Therapeutics” regarding possible drug-drug interactions (9th ed, 1996) page 51 in particular. This book teaches that “The frequency of significant beneficial or adverse drug interactions is unknown” (see the bottom of the left column of page 51) and that “Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed” and that “The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences” (see the right column of page 51) (emphases added). In the instant case, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would not be able to fully predict possible adverse drug-drug interactions occurring with many combinations of any

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compounds having claimed functional properties in the pharmaceutical compositions herein to be administered to a host. Thus, the teachings of the book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

It is noted that only four particular adrenergic $\beta 2$ receptor agonists, salbutamol, reproterol, salmeterol, and formoterol, in combination with loteprednol employed in the composition herein are shown in the working examples of the specification herein. Thus, the evidence in the examples is also not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of the active agents or compounds in the claimed composition. See MPEP § 716.02(d).

Thus, the specification fails to provide sufficient support of the broad use of any compounds having those functions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of any compounds having the function recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the Wands factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice

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the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test all compounds encompassed in the instant claims and their combinations employed in the claimed compositions to be administered to a host, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitations "tolerable" and "customary excipient" in the instant claims render claims 1-8 indefinite. The recitations "tolerable" and "customary excipient" are not clearly defined in the claims and specification. Hence, one of ordinary skill in the art could not interpret the metes and bounds of the patent protection desired as to "tolerable" and "customary excipient". Therefore, the claims are indefinite as to "tolerable" and "customary excipient" encompassed thereby.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over DOI, Koji (WO 9831343, PTO-892) and BJERKEC (PTO-1449 submitted March 29, 2002) and van der Molen (PTO-1449 submitted March 29, 2002).

Doi discloses that loteprednol etabonate is known to be useful in a pharmaceutical composition and a method of treating inflammatory conditions or allergy since loteprednol etabonate has excellent anti inflammatory and antiallergic activities and is value as a drug in an ointment or a liquid form, and loteprednol etabonate is formulated into a long-term stable liquid suspension for nasal administration (see abstract, page 1, 1st and 2nd paragraphs, Examples at page 7-11, calims 1-5).

According to Bjerkec, long-acting β 2 agonists, for example, salmeterol and formoterol, are bronchospasmolytics, are used as inhalations in asthma treatment. These long-acting β 2 agonists should always be given in combination with corticosteroids. Short-acting β 2 agonists, for example, salbutamol, may be given additionally (see abstract; page 587 'Introduction'; page 589, right-hand column, paragraph 4; page 590 'Conclusion'). The corticosteroids indicated include beclomethasone dipropionate, budesonide and fluticasone propionate (see page 588, left-hand column, lines 1-2; page 589, right-hand column, line 19).

The clinical study described in van der Molen shows that the symptoms of asthma patients are improved on inhalation of the long-acting β 2 agonist, formoterol in

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addition to inhaled corticosteroids (see abstract; page 536 'Subjects'; page 538 'Discussion'). Van der Molen does not specify the corticosteroids used.

The prior art does not expressly disclose that the employment of loteprednol etabonate in combination with reproterol, salmeterol, or formoterol in a pharmaceutical composition and a method for the treatment of allergies and/or airway disorders for simultaneous, sequential or separate administration.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ loteprednol etabonate in combination with reproterol, salmeterol, or formoterol in a pharmaceutical composition and a method for the treatment of allergies and/or airway disorders for simultaneous, sequential or separate administration.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ loteprednol etabonate in combination with reproterol, salmeterol, or formoterol in a pharmaceutical composition and a method for the treatment of allergies and/or airway disorders for simultaneous, sequential or separate administration, since both loteprednol etabonate, and reproterol, salmeterol, or formoterol, are known to be useful in a pharmaceutical composition and a method for the treatment of allergies and/or airway disorders such as asthma based on the prior art.

Therefore, one of ordinary skill in the art would have reasonably expected that combining loteprednol etabonate and reproterol, salmeterol, or formoterol both known useful for the same purpose, i.e., treating allergies and/or airway disorders such as

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asthma, would improve the therapeutic effects for treating the same diseases, and/or would produce additive therapeutic effects in treating the same.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Moreover, the teachings of Bjerkec and van der Molen have further clearly provided the motivation for the instant combination, because long-acting β 2 agonists, should always be given in combination with corticosteroids according to Bjerkec. The clinical study described in van der Molen shows that the symptoms of asthma patients are improved on inhalation of the long-acting β 2 agonist, formoterol in addition to inhaled corticosteroids. It is noted that loteprednol etabonate is the particular corticosteroid.

Further, the process for preparation of a pharmaceutical composition herein is considered well within conventional skills in pharmaceutical science.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.


In view of the rejections to the pending claims set forth above, no claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.



S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
February 18, 2004